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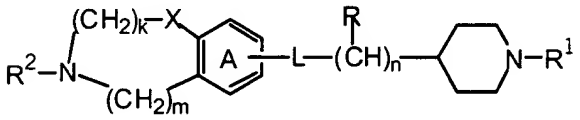
In the Abstract

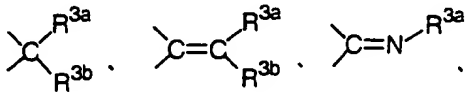
ABSTRACT

[A nitrogen] Nitrogen -containing condensed heterocyclic **[derivative of the present invention, which is a compound represented by the formula:**

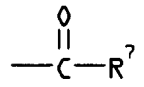


(I)

wherein ring A represents benzene ring optionally having a further substituent, -L- represents -O-, $-NR^{3a}-$, -S-, -SO-, $-SO_2-$, $-SO_2NR^{3a}-$, $-SO_2NHCONR^{3a}-$, $-SO_2NHC(=NH)NR^{3a}-$, -C(=S)-,



or $-CONR^{3a}-$ (wherein R^{3a} and R^{3b} represent independently hydrogen atom, cyano group, hydroxy group, amino group, a C_{1-6} alkyl group or a C_{1-6} alkoxy group), n represents an integer of 0 to 6, R is hydrogen atom or a hydrocarbon group optionally having a substituent, and may be different in repetition of n, R^1 represents a hydrocarbon group optionally having a substituent or a group represented by the formula:



(wherein R^7 represents a hydrocarbon group optionally having a substituent), R^2 represents hydrogen atom, an acyl group, a hydrocarbon group optionally having a

substituent or a heterocyclic group optionally having a substituent, X represents a bond, O, S, SO, SO_2 or NR^4 (wherein R^4 represents hydrogen atom, an acyl group or a hydrocarbon group optionally having a substituent), k and m represent independently an integer of 0 to 5, and l<k+m<5, or a salt thereof, and the like, has] **derivatives having** an excellent thermal production promoting activity **[and the like, and is useful as an agent]** **and their utility as agents** for preventing or treating obesity and obesity-based diseases **are disclosed**.

In the Specification

Page 20, paragraph 2 (AMENDED)

As the "substituent" in the "benzene ring optionally having a substituent" for ring A in the formulae (I) and (I'), used are, for example, (i) an optionally halogenated lower alkyl group, (ii) a halogen atom (e.g., fluorine, chlorine, bromine, iodine and the like), (iii) nitro group, (iv) cyano group, (v) hydroxy group, (vi) an optionally halogenated lower alkoxy group, (vii) amino group, (viii) a mono-lower alkylamino group (e.g., a mono-C_{1-6} alkylamino group and the like such as methylamino, ethylamino, propylamino and the like), (ix) a di-lower alkylamino group (e.g., a di-lower alkylamino group and the like such as dimethylamino, diethylamino and the like), (x) a 5 to 7 membered cyclic amino group optionally having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom in addition to one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino and the like), (xi) a lower alkyl-carbonylamino group (e.g., a C_{1-6} alkyl-carbonylamino and the like such as acetylamino, propionylamino, butyrylamino and the like), (xii) aminocarbonyloxy group, (xiii) a mono-lower alkylamino-carbonyloxy group (e.g., a mono-C_{1-6} alkylamino-carbonyloxy group and the like such as methylaminocarbonyloxy, ethylaminocarbonyloxy group), (xiv) a di-lower alkylamino-

carbonyloxy group (e.g., a di-C_{1-6} alkylaminocarbonyloxy group and the like such as dimethylaminocarbonyloxy, diethylaminocarbonyloxy and the like), (xv) a lower alkylsulfonylamino group (e.g., a C_{1-6} alkylsulfonylamino group and the like such as methylsulfonylamino, ethylsulfonylamino, propylsulfonylamino and the like), (xvi) a lower alkoxy-carbonyl group (e.g., a C_{1-6} alkoxy-carbonyl group and the like such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isobutoxycarbonyl and the like), (xvii) carboxy group, (xviii) a lower alkyl-carbonyl group (e.g., a C_{1-6} alkyl-carbonyl group and the like such as methylcarbonyl, ethylcarbonyl, butylcarbonyl and the like), (xix) carbamoyl group, (xx) a mono-lower alkyl-carbamoyl group (e.g., a mono-C_{1-6} alkyl-carbamoyl group and the like such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, butylcarbamoyl and the like), (xxi) a di-lower alkyl-carbamoyl group (e.g., a di-C_{1-6} alkyl-carbamoyl group and the like such as diethylcarbamoyl, dibutylcarbamoyl and the like), (xxii) a lower alkyl-thiocarbonyl group (e.g., a C_{1-6} alkyl-thiocarbonyl group such as methylthiocarbonyl, ethylthiocarbonyl, butylthiocarbonyl and the like), (xxiii) thiocarbamoyl group, (xxiv) a mono-lower alkyl-thiocarbamoyl group (e.g., a mono-C_{1-6} alkyl-thiocarbamoyl group and the like such as methylthiocarbamoyl, ethylthiocarbamoyl, propylthiocarbamoyl, butylthiocarbamoyl and the like), (xxv) a di-lower alkyl-thiocarbamoyl group (e.g., a di-C_{1-6} alkyl-thiocarbamoyl group and the like such as diethylthiocarbamoyl, dibutylthiocarbamoyl and the like), (xxvi) phenyl group [the (xxvi) phenyl group may have further 1 to 4 substituents, for example, selected from a lower alkyl (e.g., a C_{1-6} alkyl such as methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, hexyl and the like), a lower alkoxy (e.g., a C_{1-6} alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy and the like), halogen (e.g., fluorine, chlorine, bromine, iodine and the like), hydroxy, amino, a mono-lower alkylamino (e.g., a mono-C_{1-6} alkylamino and the like such as methylamino, ethylamino, propylamino and the like), a di-lower alkylamino (e.g., a di-C_{1-6} alkylamino and the like such as dimethylamino, diethylamino and the

like), nitro, a lower alkyl-carbonyl (e.g., a C_{1-6} alkyl-carbonyl and the like such as methylcarbonyl, ethylcarbonyl, **[buthylcarbonyl]** **butylcarbonyl** and the like)].

Page 24, paragraph 3 (AMENDED)

As the "substituent" in the "hydrocarbon group optionally having a substituent" for R^1 and R^2, used are one to five (preferably one to three) substituents selected from (i) a halogen atom (e.g., fluorine, chlorine, bromine, iodine and the like), (ii) nitro group, (iii) cyano group, (iv) oxo group, (v) hydroxy group, (vi) an optionally halogenated lower(C_{1-6})alkyl group (e.g., methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, sec-butyl, trifluoromethyl, trichloromethyl and the like), (vii) an optionally halogenated lower(C_{1-6})alkoxy group (e.g., methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butyloxy, trifluoromethoxy, trichloromethoxy and the like), (viii) an optionally halogenated lower(C_{1-6})alkylthio group (e.g., methylthio, ethylthio, propylthio, trifluoromethylthio and the like), (ix) amino group, (x) a mono-lower alkylamino group (e.g., a mono-C_{1-6} alkylamino group and the like such as methylamino, ethylamino, propylamino and the like), (xi) a di-lower alkylamino group (e.g., a di-C_{1-6} alkylamino group and the like such as dimethylamino, diethylamino and the like), (xii) a 5 to 7 membered cyclic amino group optionally having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom in addition to carbon atoms and one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino and the like), (xiii) a lower alkyl-carbonylamino group (e.g., a C_{1-6} alkyl-carbonylamino group and the like such as acetylamino, propionylamino, butyrylamino and the like), (xiv) a lower alkylsulfonylamino group (e.g., a C_{1-6} alkyl-carbonylamino group and the like such as methylsulfonylamino, ethylsulfonylamino and the like), (xv) a lower alkoxy-carbonyl group (e.g., a C_{1-6} alkoxy-carbonyl group and the like such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl and the like), (xvi) carboxyl group, (xvii) a lower alkyl-carbonyl group (e.g., a C_{1-6} alkyl-carbonyl group and the like such as

methylcarbonyl, ethylcarbonyl, propylcarbonyl and the like), (xviii) carbamoyl group, (xix) a mono-lower alkyl-carbamoyl group (e.g., a mono-C_{1-6} alkyl-carbamoyl group and the like such as methylcarbamoyl, ethylcarbamoyl and the like), (xx) a di-lower alkyl-carbamoyl group (e.g., a di-C_{1-6} alkyl-carbamoyl group and the like such as dimethylcarbamoyl, diethylcarbamoyl and the like), (xxi) a lower alkyl sulfonyl group (e.g., a C_{1-6} alkylsulfonyl group and the like such as methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like), (xxii) a lower alkoxy-carbonyl-lower alkyl group (e.g., a C_{1-6} alkoxy-carbonyl-C_{1-6} alkyl group and the like such as methoxycarbonylmethyl, ethoxycarbonylmethyl, tert-butoxycarbonylmethyl, methoxycarbonylethyl, methoxycarbonyl(dimethyl)methyl, ethoxycarbonyl(dimethyl)methyl, tert-butoxycarbonyl(dimethyl)methyl and the like), (xxiii) a carboxyl-lower alkyl group (e.g., a carboxyl-C_{1-6} alkyl group and the like such as carboxylmethyl, carboxylethyl, carboxyl(dimethyl)methyl and the like), (xxiv) a heterocyclic group optionally having a substituent, (xxv) a C_{6-14} aryl group (e.g., phenyl, naphthyl and the like), (xxvi) a C_{7-16} aralkyl group (e.g., benzyl and the like), ureido group optionally having a substituent (e.g., ureido, 3-methylureido, 3-ethylureido, 3-phenylureido, 3-(4-fluorophenyl)ureido, 3-(2-methylphenyl)ureido, 3-(4-methoxyphenyl)ureido, 3-(2,4-difluorophenyl)ureido, 3-[3,5-bis(trifluoromethyl)phenyl]ureido, 3-benzylureido, 3-(1-naphthyl)ureido, 3-(2-biphenylyl)ureido and the like), (xxviii) thioureido group optionally having a substituent (e.g., thioureido, 3-methylthioureido, 3-ethylthioureido, 3-phenylthioureido, 3-(4-fluorophenyl)thioureido, 3-(4-methylphenyl)thioureido, 3-(4-methoxyphenyl)thioureido, 3-(2,4-dichlorophenyl)thioureido, 3-benzylthioureido, 3-(1-naphthyl)thioureido and the like), (xxix) amidino group optionally having a substituent (e.g., amidino, **[N^1-methylamidiono, N^1-ethylaidino,]** **<u>N^1-methylamidino, N^1-ethylamidino,</u>** N^1-phenylamidino, N^1,N^1-dimethylamidino, N^1,N^2-dimethylamidino, N^1-methyl-N^1-ethylamidino, N^1,N^1-diethylamidino, N^1-methyl-N^1-phenylamidino, N^1,N^1-di(4-nitrophenyl)amidino and the like), (xxxx) guanidino group optionally having a substituent (e.g.,

guanidino, 3-methylguanidino, 3,3-dimethylguanidino, 3,3-diethylguanidino and the like), (xxxi) a cyclic aminocarbonyl group optionally having a substituent (e.g., pyrrolidinocarbonyl, piperidinocarbonyl, (4-methylpiperidino)carbonyl, (4-phenylpiperidino)carbonyl, (4-benzylpiperidino)carbonyl, (4-benzoylpiperidino)carbonyl, [4-(4-fluorobenzoyl)piperidino]carbonyl, (4-methylpiperazino)carbonyl, (4-phenylpiperazino)carbonyl, [4-(4-nitrophenyl)piperazino]carbonyl, (4-benzylpiperazino)carbonyl, morpholinocarbonyl, thiomorpholinocarbonyl and the like), (xxxii) aminothiocarbonyl group optionally having a substituent (e.g., aminothiocarbonyl, methylaminothiocarbonyl, dimethylaminothiocarbonyl and the like), (xxxiii) aminosulfonyl group optionally having a substituent (e.g., aminosulfonyl, methylaminosulfonyl, dimethylaminosulfonyl and the like), (xxxiv) phenylsulfonylamino group optionally having a substituent (e.g., phenylsulfonylamino, (4-methylphenyl)sulfonylamino, (4-chlorophenyl)sulfonylamino, (2,5-dichlorophenyl)sulfonylamino, (4-methoxyphenyl)sulfonylamino, (4-acetylaminophenyl)sulfonylamino, (4-nitrophenyl)phenylsulfonylamino and the like), (xxxv) sulfo group, (xxxvi) sulfino group, (xxxvii) sulfeno group, (xxxviii) a C_{1-6} alkylsulfo group (e.g., methylsulfo, ethylsulfo, propylsulfo and the like), (xxxix)a C_{1-6} alkylsulfino group (e.g., methylsulfino, ethylsulfino, propylsulfino and the like), (xxxx) a C_{1-6} alkylsulfeno group (e.g., methylsulfeno, ethylsulfeno, propylsulfeno and the like), (xxxxi) phosphono group, (xxxxii) a di-C_{1-6} alkoxyphosphoryl group (e.g., dimethoxyphosphoryl, diethoxyphosphoryl, dipropoxyphosphoryl and the like), (xxxxiii) a lower alkoxy-carbonyl-lower alkoxy group (e.g., a C_{1-6} alkoxy-carbonyl-C_{1-6} alkoxy and the like such as methoxycarbonylmethoxy, ethoxycarbonylmethoxy, tert-butoxycarbonylmethoxy, methoxycarbonylethoxy, methoxycarbonyl(dimethyl)methoxy, ethoxycarbonyl(dimethyl)methoxy, tert-butoxycarbonyl(dimethyl)methoxy and the like), (xxxxiv) a carboxyl-lower alkoxy group (e.g., a carboxyl-C_{1-6} alkoxy group and the like such as

carboxylmethoxy, carboxylethoxy, carboxyl(dimethyl)methoxy and the like), (xxxxv) a lower alkyl-thiocarbonyl group (e.g., a C_{1-6} alkyl-thiocarbonyl group such as methylthiocarbonyl, ethylthiocarbonyl, butylthiocarbonyl and the like), (xxxxvi) thiocarbamoyl group, (xxxxvii) a mono-lower alkyl-thiocarbamoyl group (e.g., a mono-C_{1-6} alkyl-thiocarbamoyl group and the like such as methylthiocarbamoyl, ethylthiocarbamoyl, propylthiocarbamoyl, butylthiocarbamoyl and the like), (xxxxviii) a di-lower alkyl-thiocarbamoyl group (e.g., a di-C_{1-6} alkyl-thiocarbamoyl group and the like such as diethylthiocarbamoyl, dibutylthiocarbamoyl and the like) and the like.

Page 28, paragraph 4 (AMENDED)

As a bicyclic heterocyclic group, for example, used is a group obtained by removing one hydrogen atom from a bicyclic hetero ring such as indole, dihydroindole, isoindole, dihydroisoindole, benzofuran, dihydrobenzofuran, benzimidazole, benzoxazole, benzisoxazole, benzothiazole, indazole, quinoline, tetrahydroquinoline, isoquinoline, tetrahydroisoquinoline, terahydro-1H-1-benzazepine, terahydro-1H-2-benzazepine, tetrahydro-1H-3-benzazepine, tetrahydrobenzoxazepine, quinazoline, tetrahydroquinazoline, quinoxaline, **[tetrahydroqunoxaline]** **tetrahydroquinoxaline**, benzodioxane, benzodioxole, benzothiazine, imidazopyridine and the like.

Page 50, paragraph 2 (AMENDED)

As a protecting group for a phenolic hydroxy group for W^2, any groups may be used as **[far]** **long** as they are **[a]** general protecting **[group]** **groups** for a phenolic hydroxy group. Specifically, for example, protecting groups described in Protective **[groups]** **Groups** in Organic Synthesis; John Wiley & Sons, Inc. and the like are used and, preferably, methyl group, benzyl group and the like are used.

Page 59, paragraph 2 (AMENDED)

As a reagent for the present chlorosulfonylation reaction, for example, chlorosulfonic acid, **[sulfryl]** **sulfuryl** chloride, sulfur dioxide-copper chloride and the like can be used. In particular, chlorosulfonic acid and the like are preferable. The amount of the chlorosulfonylating reagent used is about 1 equivalent to large excessive amount. The present reaction may be performed without a solvent or using a solvent. As a solvent when the reaction is performed using a solvent, for example, dichloromethane, 1,2-dichloroethane, carbon disulfide and the like are preferable. A reaction without a solvent is particularly preferable. The reaction temperature is preferably about -20°C to about 100°C.

Page 66, paragraph 6 (AMENDED)

As a reaction for converting **the** carbonyl group, for example, a Wittig reaction, a Horner-Wadsworth-Emmons reaction, a **[Petersol Olefinization]** **Peterson Olefination** reaction, a Knoevenagel reaction and the like are mentioned, and as a reagent, reagents which are generally used in those reactions are used.

Page 76, paragraph 5 (AMENDED)

As the "substituent" in the "benzene ring optionally having a substituent" for ring A in the formula (IA), for example, used are (i) an optionally halogenated lower alkyl group, (ii) a halogen atom (e.g., fluorine, chlorine, bromine, iodine and the like), (iii) nitro group, (iv) cyano group, (v) hydroxy group, (vi) an optionally halogenated lower alkoxy group, (vii) amino group, (viii) a mono-lower alkylamino group (e.g., a mono-C_{1-6} alkylamino group and the like such as methylamino, ethylamino, propylamino and the like), (ix) a di-lower alkylamino group (e.g., a di-C_{1-6} alkylamino group and the like such as dimethylamino, diethylamino and the like), (x) a 5

to 7 membered cyclic amino group (e.g., pyrrolidino, piperidino, morpholino, thiomorpholino and the like) optionally having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom and the like in addition to, for example, one nitrogen atom, (xi) a lower alkyl-carbonylamino group (e.g., a C_{1-6} alkyl-carbonylamino group and the like such as acetylamino, propionylamino, butyrylamino and the like), (xii) aminocarbonyloxy group, (xiii) a mono-lower alkylamino-carbonyloxy group (e.g., a mono-C_{1-6} alkylamino-carbonyloxy group and the like such as methylaminocarbonyloxy, ethylaminocarbonyloxy and the like), (xiv) a di-lower alkylamino-carbonyloxy group (e.g., a di-C_{1-6} alkylamino-carbonyloxy group and the like such as dimethylaminocarbonyloxy, diethylaminocarbonyloxy and the like), (xv) a lower alkylsulfonylamino group (e.g., a C_{1-6} alkylsulfonylamino group and the like such as methylsulfonylamino, ethylsulfonylamino, propylsulfonylamino and the like), (xvi) a lower alkoxy-carbonyl group (e.g., a C_{1-6} alkoxy-carbonyl group and the like such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isobutoxycarbonyl and the like), (xvii) carboxyl group, (xviii) a lower alkyl-carbonyl group (e.g., a C_{1-6} alkyl-carbonyl group and the like such as methylcarbonyl, ethylcarbonyl, butylcarbonyl and the like), (xix) carbamoyl group, (xx) a mono-lower alkyl-carbamoyl group (e.g., a mono-C_{1-6} alkyl-carbamoyl group and the like such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, butylcarbamoyl and the like), (xxi) a di-lower alkyl-carbamoyl group (e.g., a di-C_{1-6} alkyl-carbamoyl group and the like such as diethylcarbamoyl, dibutylcarbamoyl and the like), (xxii) a lower alkyl-thiocarbonyl group (e.g., a C_{1-6} alkyl-thiocarbonyl group and the like such as methylthiocarbonyl, ethylthiocarbonyl, butylthiocarbonyl and the like), (xxiii) thiocarbamoyl group, (xxiv) a mono-lower alkyl-thiocarbamoyl group (e.g., a mono-C_{1-6} alkyl-thiocarbamoyl and the like such as methylthiocarbamoyl, ethylthiocarbamoyl, propylthiocarbamoyl, butylthiocarbamoyl and the like), (xxv) a di-lower alkyl-thiocarbamoyl group (e.g., a di-C_{1-6} alkyl-thiocarbamoyl group and the like such as diethylthiocarbamoyl, dibutylthiocarbamoyl and the like), (xxvi) phenyl group

[the (xxvi) phenyl group may further have one to four substituents selected from, for example, a lower alkyl (a C_{1-6} alkyl and the like such as methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, hexyl and the like), a lower alkoxy (e.g., a C_{1-6} alkoxy and the like such as methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy and the like), halogen (e.g., fluorine, chlorine, bromine, iodine and the like), hydroxy, amino, **[s]** **a** mono-lower alkylamino (e.g., a mono-C_{1-6} alkylamino and the like such as methylamino, ethylamino, propylamino and the like), a di-lower alkylamino (e.g., a di-C_{1-6} alkylamino and the like such as dimethylamino, diethylamino and the like), nitro, a lower alkyl-carbonyl (e.g., a C_{1-6} alkyl-carbonyl and the like such as methylcarbonyl, ethylcarbonyl, butylcarbonyl and the like) and the like].

Page 90, paragraph 6 (AMENDED)

As Compound (IA) or a salt thereof, especially preferred are 3-[3-[1-(phenylmethyl)-4-piperidinyl]propyl]-7-(phenylmethyl)-6,7,8,9-tetrahydro-5H-isoxazolo[4,5-h][3]benzazepine; 3-[3-[1-[(2-chlorophenyl)methyl]-4-piperidinyl]propyl]-6-(phenylmethyl)-6,7,8,9- **[tetrahyro]** **tetrahydro** -5H-isoxazolo[5,4-h][2]benzazepine; or 3-[3-[1-(phenylmethyl)-4-piperidinyl]propyl]-6,7,8,9-tetrahydro-5H-isoxazolo[5,4-h][1]benzazepine or salts thereof are preferable.

Page 90, paragraph 7 (AMENDED)

As the salt of Compound (IA), physiologically acceptable salts are preferable and, physiologically acceptable acid addition salts are especially preferable. As such salts, used are, for example, salts with an inorganic acid (e.g., hydrochloric acid, phosphoric acid, hydrobromic acid, sulfuric acid), or salts with an organic acid (e.g., acetic acid, formic acid, propionic acid,

fumaric acid, maleic acid, succinic acid, tartaric acid, citric acid, malic acid, oxalic acid, benzoic acid, methanesulfonic acid, **[bensenesulfonic]** **benzenesulfonic** acid).

Page 97, paragraph 2 (AMENDED)

The present ring-closing reaction can be performed in the presence of an acid or a base as necessary. As the acid, for example, hydrochloric acid, sulfuric acid, polyphosphoric acid and the like are used. In addition, an acid anhydride such as acetic anhydride, benzoic anhydride and the like may be used. As the base, for example, sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide, rutidine, collidine, **[triethylaminde]** **triethylamine** and the like are used.

Page 125, paragraph 3 (AMENDED)

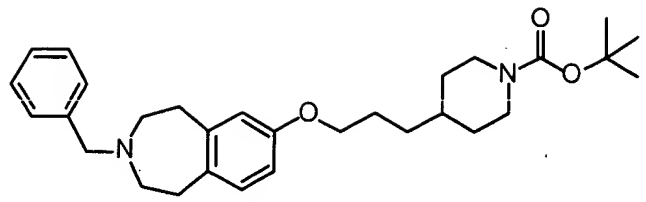
According to the same procedures as those of Reference Example 8) using t-butyl 4-[2-[[3-[(2-methylphenyl)methyl]-2,3,4,5-tetrahydro-1H-3- **[benzaepine]** **benzazepine** -7-yl]oxy]ethyl]-1-piperidinecarboxylate (0.23 g) obtained in Reference Example 9), the title compound (0.185 g) was obtained as an oil.

^{1}H NMR($CDCl_3$) δ 1.10 - 1.33 (2H, m), 1.60 - 1.83 (3H, m), 1.92 - 2.08 (2H, m), 2.39 (3H, s), 2.50 - 2.77 (7H, m), 2.78 - 2.90 (4H, m), 3.02 - 3.17 (2H, m), 3.53 (2H, s), 3.97 (2H, t, J = 5.9 Hz), 6.57 - 6.69 (2H, m), 6.98 (1H, d, J = 8.0 Hz), 7.11 - 7.22 (3H, m), 7.25 - 7.37 (1H, m).

Page 125, paragraph 4 (AMENDED)

Reference Example 11)

t-Butyl 4-[3-[[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3- **[benzaepine]** **benzazepine** -7-yl]oxy]propyl]-1-piperidinecarboxylate



Page 125, paragraph 5 (AMENDED)

According to the same procedures as those of Reference Example 7) using 7-hydroxy-3-phenylmethyl-2,3,4,5-tetrahydro-1H-3- **[benzaepine]** **benzazepine** (0.11 g) obtained in Reference Example 4), the title compound (0.17 g) was obtained as a viscous oil.

^{1}H NMR($CDCl_3$) δ 0.97 - 1.23 (2H, m), 1.30 - 1.48 (12H, m), 1.58 - 1.86 (4H, m), 2.54 - 2.77 (6H, m), 2.80 - 2.92 (4H, m), 3.63 (2H, s), 3.91 (2H, t, J = 6.4 Hz), 3.98 - 4.16 (2H, m), 6.57 - 6.66 (2H, m), 6.97 (1H, d, J = 7.7 Hz), 7.21 - 7.38 (5H, m).

Page 126, paragraph 3 (AMENDED)

According to the same procedures as those of Reference Example 8) using t-butyl 4-[3-[[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3- **[benzaepine]** **benzazepine** -7-yl]oxy]propyl]-1-piperidinecarboxylate (0.15 g) obtained in Reference Example 11), the title compound (0.11 g) was obtained as an oil.

^{1}H NMR($CDCl_3$) δ 1.03 - 1.49 (5H, m), 1.63 - 1.99 (5H, m), 2.49 - 2.69 (6H, m), 2.78 - 2.93 (4H, m), 3.01 - 3.19 (2H, m), 3.63 (2H, s), 3.90 (2H, t, J = 6.2 Hz), 6.56 - 6.68 (2H, m), 6.97 (1H, d, J = 7.7 Hz), 7.20 - 7.40 (5H, m).

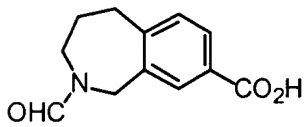
Page 126, paragraph 5 (AMENDED)

According to the same procedures as those of Reference Example 7) using 8-hydroxy-2-[(2- **[methylpheyl]** **methylphenyl**)methyl]-2,3,4,5-tetrahydro-1H-2-benzazepine (3.94 g) obtained in Reference Example 2), the title compound (4.81 g) was obtained as a viscous oil. ^{1}H NMR ($CDCl_3$) δ 1.05-1.30 (2H, m), 1.46 (9H, s), 1.60-1.80 (7H, m), 2.28 (3H, s), 2.60-2.80 (2H, m), 2.86 (2H, t-like, J = 5.4 Hz), 3.07 (2H, t-like, J = 5.2 Hz), 3.49 (2H, s), 3.81 (2H, s), 3.95 (2H, t, J = 5.8 Hz), 4.00-4.20 (2H, m), 6.54 (1H, d, J = 2.6 Hz), 6.67 (1H, dd, J = 8.0, 2.6 Hz), 7.05 (1H, d, J = 8.0 Hz), 7.10-7.30 (4H, m).

Page 141, paragraph 2 (AMENDED)

Reference Example 37)

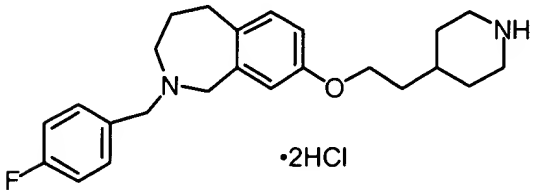
2-Formyl-2,3,4,5- **[tetrahyro]** **tetrahydro** -1H-2-benzazepine-8-carboxylic acid



Page 143, paragraph 2 (AMENDED)

Reference Example 39)

2-[(4-Fluorophenyl)methyl]-8-[2-(4-piperidinyl) **[ehtoxy]** **ethoxy**]-2,3,4,5-tetrahydro-1H-benzazepine dihydrochloride



Page 153, paragraph 2 (AMENDED)

According to the same procedures as those of Reference Example 21) using t-butyl 4-[2-[[2-(**[trifluoroaceyl]** **trifluoroacetyl**)-2,3,4,5-tetrahydro-1H-2-benzazepine-8-yl]sulfanyl]ethyl]-1-piperidinecarboxylate obtained in Reference Example 57), the title compound was obtained as a colorless oil.

^{1}H NMR ($CDCl_3$) δ 1.00-1.30 (2H, m), 1.40-1.80 (19H, m), 2.30-2.45 (1H, br), 2.55-2.80 (2H, m), 2.85-3.00 (2H, m), 3.19 (1H, t, J = 5.2Hz), 3.67 (1H, t, J = 6.4Hz), 3.90 (1H, s), 4.00-4.20 (2H, m), 7.00-7.30 (3H, m).

Page 194, paragraph 2 (AMENDED)

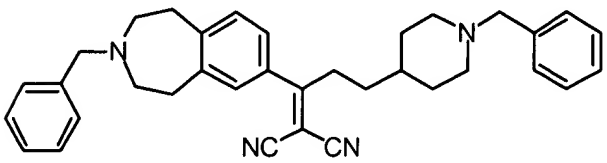
Elemental analysis for $C_{32}H_40N_4$

Calcd.: C, 79.96; H, 8.39; N, 11.66

Found: C, 79.51; H, 8.37; N, 11.46

Example 54)

2-[3-[1-(Phenylmethyl)-4-piperidinyl]-1-[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-7-yl]propylidene]malononitrile **[dihydochloride]** **dihydrochloride**



Page 196, paragraph 4 (AMENDED)

2) A solution of ethyl 3-[[4-[3-[[2-[(4-fluorophenyl)methyl]-2,3,4,5-tetrahydro-1H-2-benzazepine-8-yl]oxy]propyl]-1-piperidinyl]methyl]-1-benzenecarboxyimidate (500 mg, 0.9 mmol) obtained in 1) and 40% methylamine (methanol solution, 10 ml) in methanol (10 ml) was

heated at 120°C for 30 minutes in a stainless **steel** pressure-resistant tube. The solvent was distilled off under reduced pressure, the residue was dissolved in ethyl acetate-a 1N aqueous solution of sodium hydroxide, and extracted with ethyl acetate. After the extract was washed with an aqueous saturated solution of sodium chloride and dried with anhydrous potassium carbonate, the solvent was distilled off under reduced pressure. The resulting residue was purified by column chromatography (developing solvent: ethyl acetate- **[methonal]** **methanol** – **[NH4OH]** **NH_4OH** =1:1:0.03) using basic active alumina to obtain the title compound (512 mg) as colorless amorphous powders.

^{1}H NMR ($CDCl_3$, free base) δ 1.15-1.45 (5H, m), 1.55-2.05 (9H, m), 2.75-2.90 (4H, m), 2.98 (3H, s), 3.08 (2H, t-like, J = 5.2 Hz), 3.49 (4H, s), 3.80 (2H, s), 3.87 (2H, t, J = 6.4 Hz), 5.60-6.20 (1H, br), 6.47 (1H, d, J = 2.6 Hz), 6.66 (1H, dd, J = 8.0, 2.6 Hz), 6.90-7.05 (3H, m), 7.20-7.50 (5H, m), 7.53 (1H, s).

Page 198, paragraph 2 (AMENDED)

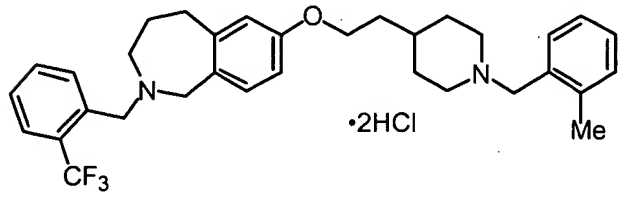
Elemental analysis for $C_{35}H_{43}FN_4O$

Calcd.: C, 75.78; H, 7.81; N, 10.10

Found: C, 75.33; H, 7.59; N, 10.05

Example 58)

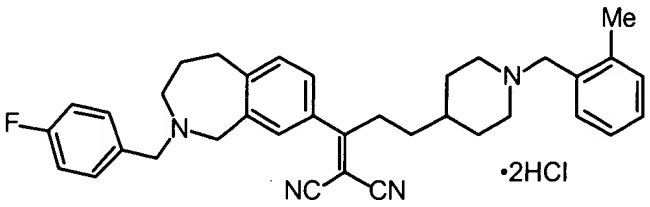
7-[2-[1-[(2-Methylphenyl)methyl]-4-piperidinyl]ethoxy]-2-[[2-(trifluoromethyl)phenyl]methyl]-2,3,4,5-tetrahydro-1H-2- **[bezazepine]** **benzazepine** dihydrochloride



Page 199, paragraph 2 (AMENDED)

Example 60)

2-[1-[2-[(4-Fluorophenyl)methyl]-2,3,4,5-tetrahydro-1H-2- **[bezazepine]** **benzazepine** -8-yl]-3-[1-[(2-methylphenyl)methyl]-4-piperidinyl]propylidene]malononitrile dihydrochloride



Page 228, paragraph 5 (AMENDED)

According to the same procedures as those of Example 46) using 2-(trifluoroacetyl)-2,3,4,5- **[terahydro]** **tetrahydro** -1H-2-benzazepine-8-sulfonyl chloride, the title compound was obtained as colorless crystals having a melting point of 131-132°C.

^{1}H NMR ($CDCl_3$) δ 1.20-2.20 (9H, m), 2.70-3.00 (4H, m), 3.10-3.15 (2H, m), 3.57 (2H, s), 3.80-4.00 (2H, m), 4.65 and 4.74 (2H, s and s), 4.80-4.95 (1H, br), 7.25-7.40 (6H, m), 7.72 (1H, dd, J = 8.0, 1.8Hz), 7.87 (1H, d, J = 1.8Hz).

Page 229, paragraph 3 (AMENDED)

According to the same procedures as those of Reference Example 21) using N-[[1-(phenylmethyl)-4-piperidinyl]methyl]-2-(trifluoroacetyl)-2,3,4,5- **[terahydro]** **tetrahydro** -1H-2-benzazepine-8-sulfonamide obtained in Example 110), the title compound was obtained as colorless crystals having a melting point of 160-162°C.

^{1}H NMR ($CDCl_3$) δ 1.10-2.00 (10H, m), 2.75-2.95 (4H, m), 2.95-3.01 (2H, m), 3.24 (2H, t-like, J = 5.2Hz), 3.49 (2H, s), 3.99 (2H, s), 4.40-4.65 (1H, br), 7.20-7.35 (7H, m), 7.55-7.65 (1H, m).

Page 239, paragraph 2 (AMENDED)

Preparation Example 1

(1) 7-[2-[1-(phenylmethyl)-4-piperidinyl]ethoxy]-3-(phenylmethyl)-2,3,4,5- **[tetrahyro]** **tetrahydro** -1H-3-benzazepine dihydrochloride (compound of Example 6)

1 g

(2) Lactose 197 g

(3) Corn starch 50 g

(4) Magnesium stearate 2 g

Page 239, paragraph 4 (AMENDED)

Preparation Example 2

(1) 7-[2-[1-(phenylmethyl)-4-piperidinyl]ethoxy]-3-(phenylmethyl)-2,3,4,5- **[tetrahyro]** **tetrahydro** -1H-3-benzazepine dihydrochloride (compound of Example 6)

2 g

(2) Lactose 197 g

(3) Corn starch 50 g

(4) Magnesium stearate 2 g

Page 240, paragraph 1 (AMENDED)

Preparation Example 3

(1) 7-[2-[1-(phenylmethyl)-4-piperidinyl]ethoxy]-3-(phenylmethyl)-2,3,4,5- **[tetrahyro]** **tetrahydro** -1H-3-benzazepine dihydrochloride (compound of Example 6)

25 g

(2) Lactose 80 g

(3) Corn starch 42 g

(4) Talc powder 3 g

(5) Magnesium stearate 0.5 g

Page 240, paragraph 4 (AMENDED)

Preparation Example 4

(1) 7-[2-[1-(phenylmethyl)-4-piperidinyl]ethoxy]-3-(phenylmethyl)-2,3,4,5- **[tetrahyro] tetrahydro** -1H-3-benzazepine dihydrochloride (compound of Example 6)

5.0 mg

(2) Lactose 60.0 mg

(3) Corn starch 35.0 mg

(4) Gelatin 3.0 mg

(5) Magnesium stearate 2.0 mg

Page 241, paragraph 4 (AMENDED)

2) Lithium aluminum hydride (1.4 g, 36.8 mmol) was added to a solution of 8-methoxy-2,3,4,5-tetrahydro-1H-3-benzazepine-2-one (3.5 g, 18.5 mmol) obtained in 1) in tetrahydrofuran (300 ml) portionwise at room temperature. After the mixture was heated at reflux for 4 hours and allowed to cool, water (2.8 ml) then a 10% aqueous solution of sodium hydroxide (2.24 ml) were added dropwise. After stirring at room temperature for 14 hours, the resulting precipitates were removed by filtration, and the solvent was distilled off under reduced pressure to obtain the crude product of 7-methoxy-2,3,4,5- **[terahydro] tetrahydro**-1H-3-benzazepine (3.0 g) as a viscous oil.

Page 241, paragraph 5 (AMENDED)

3) Trifluoroacetic acid anhydride (3.3 g, 15.7 mmol) was added dropwise to a solution of 7-methoxy-2,3,4,5- **[terahydro]** **tetrahydro** -1H-3-benzazepine (2.5 g, 14.1 mmol) obtained in 2) in tetrahydrofuran (10 ml). After the mixture was heated to 70-75°C for 1 hour, the solvent was distilled off under reduced pressure. The residue was dissolved in water-ethyl acetate and extracted with ethyl acetate. The extract was washed with an aqueous saturated solution of sodium chloride and dried with anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to obtain the residue, which was purified by silica gel column chromatography (developing solvent: hexane-ethyl acetate=5:1) to obtain the title compound (2.2 g) as an oil.

^{1}H NMR($CDCl_3$) δ 2.87-2.99(4H, m), 3.62-3.84(7H, m), 6.66-6.76(2H, m), 7.02-7.13(1H, m).

Page 244, paragraph 2 (AMENDED)

1) A mixture of 4-(1-acetyl-4-piperidinyl)-1-[7-hydroxy-3-(trifluoroacetyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-8-yl]-1-butanone (0.35 g, 0.77 mmol), **[hydroxyamine]** **hydroxylamine** hydrochloride (0.16 g, 2.3 mmol) and sodium acetate (0.19 g, 2.31 mmol) was heated in a mixed solution of water-ethanol (2/8 ml) at 80°C for 4 hours. The solvent was distilled off under reduced pressure to obtain the residue, which was dissolved in water-ethyl acetate and extracted with ethyl acetate. The extract was washed with an aqueous saturated solution of sodium chloride and dried with anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to obtain the residue, which was purified by silica gel column chromatography (developing solvent: ethyl acetate) to obtain a solid (about 0.36 g) having a melting point of 183-189°C.

Page 245, paragraph 3 (AMENDED)

1) An aqueous solution (2 ml) of potassium carbonate (50 mg) was added to a solution of 3-[3-(1-acetyl-4-piperidinyl]propyl]-7-(trifluoroacetyl)-6,7,8,9-tetrahydro-5H-isoxazolo[4,5-h][3]benzazepine (70 mg, 0.155 mmol) obtained in Example 1A) in methanol (10 ml). After the mixture was stirred at room temperature for 2 hours, the solvent was distilled off under reduced pressure. The resulting residue was dissolved in water-ethyl acetate and extracted with ethyl acetate. The extract was washed with an aqueous saturated solution of sodium chloride and dried with anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to obtain 3-[3-(1-acetyl-4-piperidinyl)propyl]-6,7,8,9- **[tetrahyro]** **tetrahydro** -5H-isoxazolo[4,5-h][3]benzazepine (52 mg) as an oil.

^{1}H NMR($CDCl_3$) δ 0.97-1.98(9H, m), 2.07(3H, s), 2.42-2.60(2H, m), 2.83-3.13(11H, m), 3.72-3.83(1H, m), 4.51-4.65(1H, m), 7.30(1H, s), 7.33(1H,s).

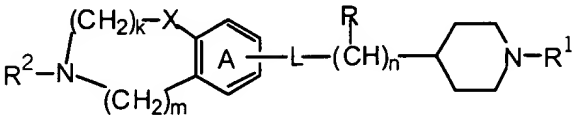
Page 246, paragraph 2 (AMENDED)

2) A mixture of 3-[3-(1-acetyl-4-piperidinyl)propyl]-6,7,8,9- **[tetrahyro]** **tetrahydro** -5H-isoxazolo[4,5-h][3]benzazepine (52 mg) obtained in 1) and concentrated hydrochloric acid (4 ml) was heated at reflux for 5 hours. After allowing to cool, the solution was made alkaline by addition of **[a]** **an** 8N aqueous solution of sodium hydroxide and extracted with ethyl acetate. The extract was washed with an aqueous saturated solution of sodium chloride and dried with anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to obtain 3-[3-(4-piperidinyl)propyl]-6,7,8,9-tetrahydro-5H-isoxazolo[4,5-h][3]benzazepine (40 mg) as an oil. This oil became solid having a melting point of 186-190°C upon allowing to stand at room temperature.

^{1}H NMR($CDCl_3$) δ 0.97-1.53(7H, m), 1.62-1.96(4H, m), 2.12-2.42(2H, br), 2.48-2.67(2H, m), 2.82-3.15(10H, m), 7.29(1H, s), 7.33(1H,s).

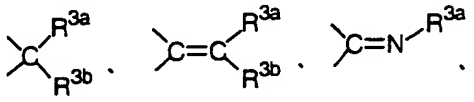
In the Claims

1. (Once Amended) A compound represented by the formula:

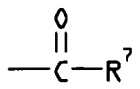


(I)

wherein ring A represents benzene ring optionally having a further substituent, -L- represents -O-, $-NR^{3a}-$, -S-, -SO-, $-SO_2-$, $-SO_2NR^{3a}-$, $-SO_2NHCONR^{3a}-$, $-SO_2NHC(=NH)NR^{3a}-$, -C(=S)-,



or $-CONR^{3a}-$ [(]wherein R^{3a} and R^{3b} represent independently hydrogen atom, cyano group, hydroxy group, amino group, a C_{1-6} alkyl group or a C_{1-6} alkoxy group[)], n represents an integer of 0 to 6, R is hydrogen atom or a hydrocarbon group optionally having a substituent, and may be different in repetition of n, R^1 represents a hydrocarbon group optionally having a substituent or a group represented by the formula:



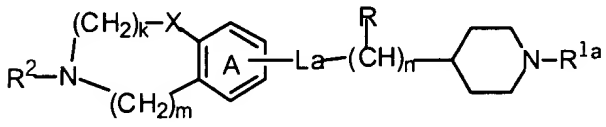
[(]wherein R^7 represents a hydrocarbon group optionally having a substituent, R^2 represents hydrogen atom, an acyl group, a hydrocarbon group optionally having a substituent or a heterocyclic group optionally having a substituent, X represents a bond, **[O, S, SO, SO_2 or NR^4**

(wherein R^4 represents hydrogen atom, an acyl group or a hydrocarbon group optionally having a substituent), k and m represent independently an integer of 0 to 5, and 1<k+m<5,] **k and m are each independently an integer of 0 to 4 and k + m = 4,** or a salt thereof.

12. (Once Amended) **[The compound according to claim 1, which is (i)]** **A compound selected from the group consisting of** 2-[(2-methylphenyl)methyl]-7-[2-[1-[[2-(trifluoromethyl)phenyl]methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(ii)]** 2-[(2-methylphenyl)methyl]-8-[2-[1-[(4-chlorophenyl)methyl **[)]]** -4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(iii) 1-(4-pyridyl)-5-[1-hydroxy-3-[1-(phenylmethyl)-4-piperidinyl]propyl]-2,3-dihydroindole, (iv)]** 3-[1-(phenylmethyl]-4-piperidinyl]-1-[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-7-yl]-1-propanone oxime, **[(v)]** 2-[1-[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-7-yl]-3-[1-(phenylmethyl)-4-piperidinyl]propylidene]malononitrile, **[(vi)]** 3-(phenylmethyl)-7-[[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]sulfanyl]-2,3,4,5-tetrahydro-1H-3-benzazepine, **[(vii)]** 7-[[2-[1-[(2-chlorophenyl)methyl]-4-piperidinyl]ethyl]sulfinyl]-3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine, **[(viii)]** 7-[[2-[1-[(4-chlorophenyl)methyl]-4-piperidinyl]ethyl]sulfinyl]-3-(phenylmethyl)-2,3,4**[.] ,** 5-tetrahydro-1H-3-benzazepine, **[(ix)]** 7-[[2-[1-[(3-chlorophenyl)methyl]-4-piperidinyl]ethyl]sulfonyl]-3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine, **[(x)]** 8-[3-[1-[[3-(4,5-dihydro-1H-2-imidazolyl)phenyl]methyl]-4-piperidinyl]propoxy]-2-[(4-fluorophenyl)methyl]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(xi)]** 4-[[4-[2-[[2-[(2-methylphenyl)methyl]-2,3,4,5-tetrahydro-1H-2-benzazepine-8-yl]oxy]ethyl]-1-piperidinyl]methyl]-1-benzenecarboxyimidamide, **[(xii)]** 8-[2-[1-[[4-(4,5-dihydro-1H-2-imidazolyl)phenyl **[)]]** methyl]-4-piperidinyl]ethoxy]-2-[(2-methylphenyl)methyl]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(xiii)]** 2-(phenylmethyl)-8-[2-[1-[[4-(N,N-diethylaminomethyl)phenyl]methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-

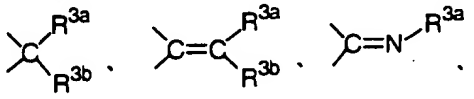
benzazepine, **[(xiv)]** 2-[(2-methylphenyl)methyl]-8-[2-[1-[[3-(4,5-dihydro-1H-2-imidazolyl)phenyl]methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(xv)]** 2-[(2-methylphenyl)methyl]-8-[2-[1-[4-(4,5-dihydro-1H-2-imidazolyl)benzoyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2- **[benazepine]** **benzazepine**, **[(xvi)]** 2-(phenylmethyl)-7-[[1-[[4-(4,5-dihydro-1H-2-imidazolyl)phenyl]methyl]-4-piperidinyl]methoxy]-2,3,4,5-tetrahydro-1H-2- **[benazepine]** **benzazepine**, **[(xvii)]** 2-(phenylmethyl)-8-[[1-[[4-(4,5-dihydro-1H-2-imidazolyl)phenyl]methyl]-4-piperidinyl]methoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[(xviii)]** 2-(phenylmethyl)-8-[2-[1-[[4-(4,5-dihydro-1H-2-imidazolyl)phenyl]methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, **[or (xix)]** **and** 2-(phenylmethyl)-8-[2-[1-[(4-dimethylaminophenyl)methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine, or a salt thereof.

15. (Once Amended) A compound represented by the formula:



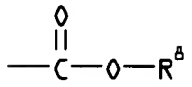
(I')

wherein ring A represents benzene ring optionally having a further substituent, **[-L^a-]** **–La-** represents $-NR^{3a}-$, -S-, -SO-, $-SO_2-$, $-SO_2NR^{3a}-$, $-SO_2NHCONR^{3a}-$, $-SO_2NHC(=NH)NR^{3a}-$, -C(=S)-,



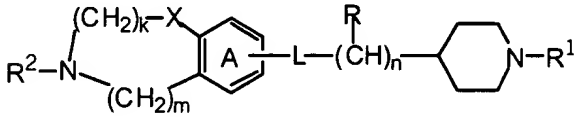
or $-CONR^{3a}-$ **[(]**wherein R^{3a} and R^{3b} represent independently hydrogen atom, cyano group, hydroxy group, amino group, a C_{1-6} alkyl group or a C_{1-6} alkoxy group**[)]**, n represents an integer of 0 to 6, R is hydrogen atom or a hydrocarbon group optionally having a substituent, and may

be different in repetition of n, R^{1a} represents hydrogen atom or a group represented by the formula:



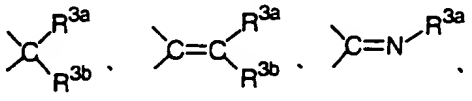
[(]wherein R^8 represents a hydrocarbon group optionally having a substituent[)], R^2 represents hydrogen atom, an acyl group, a hydrocarbon group optionally having a substituent or a heterocyclic group optionally having a substituent, X represents a bond, **[O, S, SO, SO_2 or NR^4 (wherein R^4 represents hydrogen atom, an acyl group or a hydrocarbon group optionally having a substituent), k and m represent independently an integer of 0 to 5, 1<k+m<5,]** **k and m are each independently an integer of 0 to 4 and k + m = 4,** or a salt thereof.

17. (Once Amended) A pharmaceutical composition comprising a compound represented by the formula:



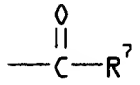
(I)

wherein ring A represents benzene ring optionally having a further substituent, -L- represents -O-, $-NR^{3a}-$, -S-, -SO-, $-SO_2-$, $-SO_2NR^{3a}-$, $-SO_2NHCONR^{3a}-$, $-SO_2NHC(=NH)NR^{3a}-$, -C(=S)-,



or $-CONR^{3a}-$ [(]wherein R^{3a} and R^{3b} represent independently hydrogen atom, cyano group, hydroxy group, amino group, a C_{1-6} alkyl group or a C_{1-6} alkoxy group[)], n represents an integer of 0 to 6, R is hydrogen atom or a hydrocarbon group optionally having a substituent, and may

be different in repetition of n, R^1 represents a hydrocarbon group optionally having a substituent or a group represented by the formula:



[(]wherein R^7 represents a hydrocarbon group optionally having a substituent[)], R^2 represents hydrogen atom, an acyl group, a hydrocarbon group optionally having a substituent or a heterocyclic group optionally having a substituent, X represents a bond, **[O, S, SO, SO_2 or NR^4 (wherein R^4 represents hydrogen atom, an acyl group or a hydrocarbon group optionally having a substituent), k and m represent independently an integer of 0 to 5, and 1<k+m<5,]** **k and m are each independently an integer of 0 to 4 and k + m = 4,** or a salt thereof or a prodrug thereof

and a pharmacologically acceptable carrier.

REMARKS

I. Amendments

Claims 1, 12, 15 and 17 have been amended; and claims 6, 16, 18-21, 23-41 and 42 have been canceled.

Typographical and grammatical errors have also been corrected throughout the specification.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version with Markings to Show Changes Made".

As the Applicants have previously indicated, a change of inventorship is necessitated by the imposed restriction requirement. A request to modify inventorship has previously been submitted.

II. Discussion of the Restriction Requirement

In the Office Action dated June 24, 2002 (Paper No. 5), the Examiner imposed a restriction requirement. Applicants hereby confirm their election of Group I, including claims 1-5, 7-15, 17-23, 43 and 44.

By this amendment, Applicants have cancelled withdrawn claims 6, 16 and 24-42 without prejudice to the filing of future continuing applications.

Additionally, Applicants have amended independent claims 1, 15 and 17 so that the definitions of X, m and k conform to the restriction requirement.

This amendment adds no new matter to the specification. Support may be found in the claims as originally filed. Moreover, support for "k and m are each independently an integer of 0 to 4 and k + m = 4" is found in the specification at page 36, lines 15-20 *inter alia*.

Furthermore, by this amendment, claim 12 has been amended to delete the non-benzazepine compound (formerly choice (iii)) in accordance with the restriction requirement, as well as being made independent.

Therefore, Applicants submit that the claims as amended are now in conformance with the restriction requirement.

III. Discussion of the Rejection for Improper Markush Grouping

Claims 1-3, 7-15, 17-23, 43 and 44 have been rejected as being drawn to improper Markush groups.

In conformance with the restriction requirement, independent claims 1, 15 and 17 have been amended to recite the limitations for k and m wherein k and m are each independently an integer of 0 to 4 and k + m = 4; and the limitation for X as representing a bond. With these limitations, the ring to the left of ring A is a benzazepine ring, as required for the elected Group I.

Additionally, by this amendment, claim 12 has been amended to delete the non-benzazepine compound (formerly choice (iii)) in accordance with the restriction requirement, as well as being made independent.

These amendments add no new matter to the specification, as indicated in Sec. II above. Therefore, Applicants respectfully submit that the definitions of X, k and m are now in accordance with the imposed restriction requirement for the claims as amended.

Claims 18-21 and 23 have been cancelled.

Claims 2, 3, 7-11, 13, 14, 22, 43 and 44 depend upon claim 1. Applicants submit that the more specific dependent claims are also in accordance with the restriction requirement as explained with respect to claim 1 as amended.

Therefore Applicants respectfully request withdrawal of the rejection for improper Markush grouping.

IV. Discussion of the Reminder Concerning the Abstract

The Examiner has provided a reminder stating the proper language and format for the Abstract.

A replacement Abstract, provided on a separate sheet of paper, accompanies this amendment. Therefore, Applicants submit that the Abstract is in conformance with US PTO requirements.

V. Discussion of the Rejection of Claim 13 under 35 U.S.C. Sec. 112, First Paragraph

Claims 13 has been rejected under 35 U.S.C. Sec. 112, first paragraph, as allegedly non-enabled with respect to the term "pro-drug".

Pro-drugs are defined in detail in the specification at page 40, line 12 – page 41, line 15 *inter alia*. Thus, there is guidance in the specification detailing which modifications may be made at which portions of the molecule to provide the recited pro-drugs. Applicants therefore assert that the term "pro-drug" is adequately enabled.

Moreover, Applicants wish to point out to the Examiner that claim 17 also includes the objected-to term.

Applicants respectfully submit that the argument provided above to support the enablement of the term "pro-drug" should also be applied to claim 17 in the event the Examiner should wish to reject claim 17 for this same reason.

Moreover, claim 17 has been modified to recite pharmacologically acceptable carriers in accordance with the teaching of the specification at page 116, line 17 – page 117, line 35 *inter alia*.

Therefore, Applicants respectfully request withdrawal of the Sec. 112, first paragraph rejection.

VI. Discussion of the Rejection under 35 U.S.C. Sec. 112, Second Paragraph

Claims 1-5, 7, 8, 10, 12, 13, 14, 22, 23, 43 and 44 have been rejected under 35 U.S.C. Sec. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner has objected to the following claim language: 1) the formula $-C(=O)-R^7$ of claims 1-

5, 7, 8, 10, 13, 14, 17-22, 23, 43 and 44; 2) punctuation of claims 1-5, 7, 8, 10, 13, 14, 22, 23, 43 and 44; 3) the formula >C=N-OH in claim 3; 4) punctuation, alleged insufficient antecedent basis and spelling errors in claim 12; 5) the variable La and the formula $-C(=O)-R^8$ in claim 15; 6) alleged duplication of claim 17 by claims 18-21 and 7) allegedly improper use claim 23. Each aspect of the rejection will be discussed separately below.

As to the first aspect of the rejection (Examiner's comments a and k), the partial structure $-C(=O)-R^7$ recited in independent claims 1 and 17 clearly contains an O for oxygen, and not a zero. The width of the O is the same as the width of the C in this partial formula. Had it been a zero, the width of the character would be less than the width of the C. The partial formula which the Examiner has referred to would be understood by those skilled in the art to contain a carbonyl group, as it contains the letter O and not a zero. The Applicants respectfully request that the Examiner reconsider and withdraw the first aspect of the rejection.

As to the second aspect of the rejection (Examiner's comment b), extraneous parentheses have been removed from claims 1, 15 and 17 by this amendment. Applicants submit that the second aspect of the rejection has been overcome.

As to the third aspect of the rejection (Examiner's comment c), the partial structure >C=N-OH recited in claim 3 clearly contains an O for oxygen, and not a zero. The width of the O is the same as the width of the N in this partial formula. Had it been a zero, the width of the character would be less than the width of the N. The partial formula which the Examiner has referred to would be understood by those skilled in the art to contain a hydroxy group, as it contains the letter O and not a zero. The Applicants respectfully request that the Examiner reconsider and withdraw the third aspect of the rejection.

As to the fourth aspect of the rejection (Examiner's comments d-g), claim 12 has been modified by this amendment to remove reference numerals, and to correct the misspelling of "benzazepine". As to the alleged lack of antecedent basis in species (xii), the Applicants respectfully disagree, as the "[4-(N,N-diethylaminomethyl)phenyl]methyl]" portion of the molecule corresponds to R^1 in claim 1, wherein R^1 is a group which may be a hydrocarbon group optionally having a substituent. Moreover, Applicants have made claim 12 an independent claim to ensure its separate consideration by the Examiner, so any issues of antecedent basis should now be moot. In addition, the former second and twelfth options have had punctuation corrected by this amendment. Therefore, Applicants submit that all objects related to claim 12 have been overcome by these amendments.

As to the fifth aspect of the rejection (Examiner's comments h-j) claim 15 has been modified by this amendment to recite –La- rather than $-L^a-$, to be consistent with the formula of the claim. The partial structure $-C(O)-O-R^8$ recited in claim 15 clearly contains two O's for oxygens, and not zeroes. The width of the O is the same as the width of the C in this partial formula. Had it been a zero, the width of the character would be less than the width of the C. The partial formula which the Examiner has referred to would be understood by those skilled in the art to contain a carboxy group, as it contains two letter O and not two zeroes. The Applicants respectfully request that the Examiner reconsider and withdraw this aspect of the rejection.

As to the sixth aspect of the rejection (Examiner's comment l), claims 18-21 have been cancelled by this amendment. Therefore Applicants submit that this aspect of the rejection has been overcome.

As to the seventh aspect of the rejection (Examiner's comment m), claim 23 has been cancelled by this amendment. Therefore Applicants submit that this aspect of the rejection has been overcome.

Therefore Applicants respectfully request withdrawal of the Sec. 112, second paragraph rejection.

VII. Discussion of the Rejection of Claim 23 Under 35 U.S.C. Sec. 101

Claim 23 has been rejected under 35 U.S.C. Sec. 101 as an allegedly improper use claim. By this amendment, Applicants have cancelled claim 23.

Therefore Applicants respectfully request withdrawal of the Sec. 101 rejection.

VIII. **Conclusion**

Reconsideration of the claims as amended and allowance is requested. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, the Examiner is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

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